

## **REMARKS**

The above amendments to the above-captioned application along with the following remarks are being submitted as a full and complete response to the Official Action dated January 22, 2001, the period for response to which will expire on June 22, 2000.

In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

Claims 1-4, 6-8, 11, 19, 20, 22, 24, 28 and 29 are under consideration in this application. Claims 5, 21, 23, 25, 26 and 27 are being canceled without prejudice or disclaimer, and claims 1, 2, 4, 6 - 8, 11, 19, 20, 22, 24 and 28 are being amended, as set forth above and in the attached marked-up presentation of the claim amendments, in order to more particularly define and distinctly claim applicants' invention. Applicants hereby submit that no new matter is being introduced into the application through the submission of this response.

### **35 U.S.C. §112 Rejection**

Claims 1-8, 11 and 19 - 29 were rejected under the second paragraph of 35 U.S.C. § 112, second paragraph, for various informalities outlined in the Office Action. As indicated above, the claims have been amended so that the rejection should be obviated. Accordingly, the withdrawal of the outstanding indefiniteness rejection under 35 U.S.C. §112 is in order, and is therefore respectfully solicited.

As noted by the Examiner, no prior art has been applied against the present invention. However, Applicants would nonetheless contend that the present invention as now claimed is distinguishable and thereby allowable over the prior art as a whole.

The present invention is characterized in extracting a plurality of different genomic DNA nucleotide sequences (line 10, page 6) from the human genome (line 15, page 5); extracting a plurality of partial sequences from the different genomic DNA sequences which (1) meet extraction conditions (such as a predetermined base length, GC content or Tm), and (2) are extracted from different exons (associated with certain genetic functions or diseases; lines 18-19, page 5); taking a plurality pairs of primers from the partial sequences; and synthesizing the primers, while collating the pairs of primers with the partial sequences from which the primers were derived and the corresponding DNA nucleotide sequences from which the partial sequences were extracted. The base length is one of the extraction conditions executed independently from the conditions of GC content and Tm (Fig.5; p. 20).

Since a plurality of genomic DNA nucleotide sequences are extracted into a plurality of partial sequences, which are extracted from different exons, and then a plurality of primers are thereby determined, the present invention eliminates the possibility of repeating the extracting of the same exon twice such that the desired analysis of the primers and the relevant biological functions becomes more efficient (pages 2-6). As a result, the throughputs of the amplification and analysis are significantly improved by reducing redundant processing on the same primers. The present invention applies methods, such as computerized homology exclusion (Fig. 4) to reduce cross hybridization as much as possible. The partial sequences are not cross-hybridized so as to keep the associated genetic functions separated. As such, the genetic function(s) of a specific gene is provided as a result of predicted exons and homology exclusion between cDNA and known genes. Via the present invention, it becomes possible to design a plurality of potential primers without having to be limited to only one target DNA (Fig. 8; page 4, lines 21 to page 5).

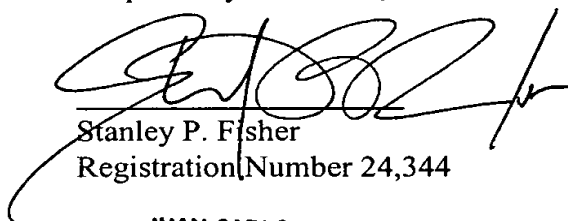
In Embodiment 2 of the present invention, five conditions (page 35, lines 3-7) are used for screening the exons on genomic DNAs, positioning exons in genomic DNAs, and collating the exons with genetic functions via some off-the-shelf databases known to one skilled in the art. For example, GENSCAN, GRILL, or RE (page 18, line 9) may be used as an exon predicting program 304, ACTION may be used for ensuring the sequence of interest is in the expressed sequence tag (EST) database and can be expressed, and SWIS-PROT is used as a protein database. The genetic functions collated with the exons are further associated with the primers by tracking ID codes (line 5, page 29). In the case of cDNAs, exon prediction is not necessary since cDNAs are ligated from exons (Fig. 3; lines 24-27, page 17). The whole method of the present invention, especially the collating step, is performed "automatically" contrary to the prior art that taught that two or more genetic functions can be "manually" collated with their corresponding pairs of primers.

In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art references upon which the rejections in the Office Action rely, Applicants respectfully contend that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application as amended is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution

and allowance of the above-captioned application, the Examiner is invited to contact the Applicants' undersigned representative at the address and phone number indicated below.

Respectfully submitted,



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**Marked-up Version of Amended Claims**

1. A primer design system, comprising:

means for selecting a plurality of different DNA nucleotide sequences from a database including a plurality of different DNA nucleotide sequences of the human [genomes] genome; and

a control unit for controlling the system, said control unit controlling:

means for extracting a plurality of partial sequences meeting extraction conditions from the plurality of different DNA nucleotide sequences, wherein said extraction conditions [including] include a predetermined base length, the database including exons identified for the DNA nucleotide sequences stored therein;

means for determining positions of said plurality of partial sequences related to each one of said different DNA nucleotide sequences, each of said plurality of different partial sequences being extracted from different exons of the same gene;

means for selecting a plurality of different partial sequences from said plurality of partial sequences based on results of said position determining means [for determining];

means for determining a plurality of pairs of primers for normal PCR for each of said plurality of different partial sequences; and

means for automatically collating said plurality of pairs of primers with [genetic functions related to] said different DNA nucleotide sequences [respectively] from which said plurality of different partial sequences used to determine said plurality of pairs of primers were extracted.

2. A primer design system according to claim 1, wherein said control unit further controls a second means for selecting a plurality of primers meeting certain selection conditions from said plurality of partial sequences extracted by said extracting means after selecting a plurality of different partial sequences.
4. A primer design system according to claim 1, wherein said control unit further controls means for limiting the plurality of [mutually] different DNA nucleotide sequences, the

data for which were obtained by said selecting means, to a base length longer than said [certain] predetermined base length, to be output to said extracting means.

6. A primer design system according to claim 1, further comprising a second database including data on a plurality of different DNA nucleotide sequences, said second database comprising at least one of [either] data on cDNA nucleotide sequences included in said first database[, or] and data on the exon nucleotide sequences predicted on the basis of genomic DNA nucleotide sequences included in said first database, wherein said extracting means targets nucleotide sequences included in said second database for extraction.
7. A storage medium having recorded thereon a program executable at a control unit in a computer with memory recording data on a plurality of different DNA nucleotide sequences of the human [genomes] genome, said program comprising instructions
  - for reading data on a plurality of different DNA nucleotide sequences in said memory,
  - for extracting a plurality of partial sequences meeting extraction conditions from said plurality of different DNA nucleotide sequences and the data on said plurality of different DNA nucleotide sequences, wherein said extraction conditions [including] include a predetermined base length, the data on said plurality of different DNA nucleotide sequences including exons identified for the DNA nucleotide sequences,
  - for determining positions of said plurality of partial sequences related to each one of said different DNA nucleotide sequences, each of said plurality of different partial sequences being extracted from different exons of the same gene,
  - for selecting a plurality of different partial sequences from results of the determining step, and
  - for determining a plurality pairs of primers for normal PCR for each of said plurality of different partial sequences, and
  - for automatically collating said plurality of pairs of primers with [genetic functions related to] said different DNA nucleotide sequences from which said plurality of different partial sequences used to determine said plurality of pairs of primers were extracted.

8. A method for designing primers, comprising the steps of:

(a) taking data on a plurality of different DNA nucleotide sequences from a database including a plurality of different DNA nucleotide sequences of the human [genomes] genome;

(b) extracting a plurality of partial sequences meeting extraction conditions from each of said plurality of different DNA nucleotide sequences based on said data, wherein said extraction conditions [including] include a predetermined base length, said data including exons identified for the plurality of DNA nucleotide sequences;

(c) determining positions of said plurality of partial sequences related to each one of said plurality of different DNA nucleotide sequences;

(d) selecting a plurality of different partial sequences from said plurality of partial sequences, each of said plurality of different partial sequences being extracted from different exons of the same gene;

(e) after the step (d), determining a plurality pairs of primers for normal PCR for each of said plurality of different partial sequences, and

(f) automatically collating said plurality of pairs of primers with [genetic functions related to] said different DNA nucleotide sequences from which said plurality of different partial sequences used to determine said plurality of pairs of primers were extracted.

11. A method for designing primers, comprising the steps of

(a) taking data on a plurality of different DNA nucleotide sequences from a database including a plurality of DNA nucleotide sequences of the human [genomes] genome;

(b) extracting a plurality of partial sequences meeting extraction conditions from each of said plurality of different DNA nucleotide sequences based on said data, wherein said extraction conditions [including] include a predetermined base length, the database including exons identified for the DNA nucleotide sequences stored therein;

(c) determining certain conditions related to positions of said plurality of partial sequences related to each one of said plurality of different DNA nucleotide sequences;

(d) selecting a plurality of different partial sequences from said plurality of partial sequences; each of said plurality of different partial sequences being extracted from different exons of the same gene;

(e) after the step (d), determining a plurality pairs of primers for normal PCR for each of said plurality of different partial sequences; and

(f) analyzing a sample DNA using as an indicator for the type of primer affording PCR amplified fragments among said plurality of primers with a storage medium,

wherein said storage medium comprises recorded data on said plurality pairs of primers, genetic data on DNA fragments amplified by PCR using said plurality pairs of primers, and said plurality of pairs of primers automatically collated with [genetic functions related to] said different DNA nucleotide sequences from which said plurality of different partial sequences used to determine said plurality of pairs of primers were extracted.

19. A primer design system, comprising:

means for selecting a plurality of different DNA nucleotide sequences based on at least one predetermined genetic function of interest from a database having data on a plurality of DNA nucleotide sequences of the human [genomes] genome; and

a control unit for controlling the system, said control unit controlling:

means for extracting a plurality of partial sequences meeting certain base length extraction conditions from the plurality of different DNA nucleotide sequences, the database including exons identified for the DNA nucleotide sequences stored therein;

means for determining positions of said plurality of partial sequences related to each one of said plurality of different DNA nucleotide sequences;

means for selecting a plurality of different partial sequences from said plurality of partial sequences, each of said plurality of different partial sequences being extracted from different exons of the same gene; and

means for determining a plurality pairs of primers for normal PCR for each of said plurality of different partial sequences; and

means for automatically collating said plurality of pairs of primers with [said genetic functions of interest related to] said different DNA nucleotide sequences [respectively] from which said plurality of different partial sequences used to determine said plurality of pairs of primers were extracted.

20. A primer design system, comprising:

means for selecting a plurality of different DNA nucleotide sequences from a database including a plurality of DNA nucleotide sequences of the human [genomes] genome; and

a control unit for controlling the system, said control unit controlling:

means for [positioning] associating exons [associated with genetic functions of interest on] with corresponding regions in each of the plurality of different DNA nucleotide sequences;

means for extracting a plurality of partial sequences from the exons under extraction conditions, wherein said extraction conditions [including] include a predetermined base length, the database including exons identified for the DNA nucleotide sequences stored therein;

means for collating positions of said plurality of partial sequences related to each of the exons [and the genetic functions];

means for selecting a plurality of different partial sequences from said plurality of partial sequences based on results of said means for collating positions of said plurality of partial sequences, wherein more than one partial sequence is associated with a genomic sequence;

means for determining a plurality of pairs of primers for normal PCR for each of said plurality of different partial sequences; and

means for automatically collating said plurality of pairs of primers with [the genetic functions and] at least the positions related to said different DNA nucleotide sequences from which said plurality of different partial sequences used to determine said plurality of pairs of primers were extracted [respectively].



22. A storage medium having recorded thereon a program executable at a control unit in a computer with memory recording data on a plurality of different DNA nucleotide sequences of the human [genomes] genome, said program comprising instructions
- for reading data on a plurality of different DNA nucleotide sequences in said memory;
  - for positioning exons associated with genetic functions of interest on the plurality of different DNA nucleotide sequences;
  - for extracting a plurality of partial sequences from the exons under extraction conditions, wherein said extraction conditions [including] include a predetermined base length;
  - for collating positions of said plurality of partial sequences related to each of the exons and the genetic functions;
  - for selecting a plurality of different partial sequences from said plurality of partial sequences based on results of said means for collating positions of said plurality of partial sequences;
  - for determining a plurality of pairs of primers for normal PCR for each of said plurality of different partial sequences; and
  - for automatically collating said plurality of pairs of primers with [the genetic functions and] at least the positions related to said different DNA nucleotide sequences from which said plurality of different partial sequences used to determine said plurality of pairs of primers were extracted [respectively].
24. A method for designing primers, comprising:
- (a) selecting a plurality of different DNA nucleotide sequences from a database including a plurality of DNA nucleotide sequences of the human [genomes] genome;
  - (b) positioning exons associated with genetic functions of interest on the plurality of different DNA nucleotide sequences;
  - (c) extracting a plurality of partial sequences from the exons under extraction conditions, wherein said extraction conditions [including] include a predetermined base length;
  - (d) collating positions of said plurality of partial sequences related to each of the exons and the genetic functions;

(e) selecting a plurality of different partial sequences from said plurality of partial sequences based on results of said means for collating positions of said plurality of partial sequences;

(f) determining a plurality of pairs of primers for normal PCR for each of said plurality of different partial sequences; and

(g) automatically collating said plurality of pairs of primers with [the genetic functions and] at least the positions related to said different DNA nucleotide sequences [respectively] from which said plurality of different partial sequences used to determine said plurality of pairs of primers were extracted.

28. A primer design system, comprising:

means for selecting a plurality of different DNA nucleotide sequences based on at least one predetermined genetic function of interest from a database having data on a plurality of DNA nucleotide sequences of the human [genomes] genome; and

a control unit for controlling the system, said control unit controlling:

means for positioning exons associated with the genetic function of interest on the plurality of different DNA nucleotide sequences;

means for extracting a plurality of partial sequences from the exons under extraction conditions, wherein said extraction conditions [including] include a predetermined base length;

means for collating positions of said plurality of partial sequences related to each of the exons and the genetic functions;

means for selecting a plurality of different partial sequences from said plurality of partial sequences based on results of said means for collating positions of said plurality of partial sequences;

means for determining a plurality of pairs of primers for normal PCR for each of said plurality of different partial sequences; and

means for automatically collating said plurality of pairs of primers with [the genetic functions and] at least the positions related to said different DNA nucleotide sequences [respectively] from which said plurality of different partial sequences used to determine said plurality of pairs of primers were extracted.